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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,945	06/15/2001	Victor Lyamichev	FORS-04586	9139

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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/882,945	Lyamichev
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 21, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *0503*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-6, 10-18, 22-31, and 35-43 are rejected under 35 U.S.C. 102 (b) as being anticipated by Kim et al. (U.S. Patent 5,846,723) (December 8, 1998).

Kim et al teach a method for selecting a primer (Example 1), comprising:

a) providing:

I) a target nucleic acid having at least one accessible site and at least one inaccessible site (Column 11, lines 4-16 and Claims 1 and 21);

ii) a plurality of extension primers, each of the primers comprising a first region, wherein the first region of the plurality of primers differ in sequence from each other, and wherein the plurality of primers comprise first regions that are complementary to different portions of the target nucleic acid (Example 1 and Claim 36); and

iii) a template-dependent nucleic acid extension agent (Example 1, Column 11, line 30 to Column 12, line 19) and ;

b) exposing the plurality of extension primers and the extension agent to the target nucleic acid under conditions wherein primers comprising first regions that are complementary only to an inaccessible site in the target nucleic acid are not extended by the extension reagent, and wherein primers comprising first regions that are complementary to at least one accessible site of the target nucleic acid from an extension product (Example 1 and Figure 1);

c) selecting a primer complementary to at least one accessible site by identifying a member of the plurality of primers that forms an extension product (Example 1 and claims 26-29).

Kim et al teach a method, wherein the target nucleic acids comprise DNA and RNA (Examples 1 and 2 and Column 10, lines 5-9 and Claim 37).

Kim et al teach a method, wherein the plurality of primers further comprise a second region, the second region located 5' of the first region (Claim 36).

Kim et al teach a method, wherein the second regions of the plurality of primers, are identical in sequence to one another (Claim 36)

Kim et al teach a method, further comprising providing:

I) first and second amplification primers, the first amplification primer complementary to at least a portion of the second regions of the plurality of extension primers and the second amplification primer capable of hybridizing to a sequence complementary to a first domain of the target nucleic acid (Claim 36); and

ii) an amplification agent;

and further comprising the step of treating the extension products with the first and second amplification primers and the amplification agents to produce amplification products prior to the selecting step (Example 1 and Figure 1 and Column 11, line 30 to Column 12, line 19)

Kim et al teach a method, wherein the plurality of primers comprise a sufficient number of primers to encompass every sequence variation within the first region (Examples 1 and 2 and Claim 36 and Claims 21-23).

Kim et al teach a method, wherein the first region is six or more nucleotides in length (Claim 36).

Kim et al teach a method, wherein the template-dependent nucleic acid extension agent comprises a polymerase and reverse transcriptase (Example 1, Column 11, line 30 to Column 12, line 19)

Kim et al teach a composition comprising an oligonucleotide, the oligonucleotide comprising a sequence of a first region of a selected primer (Table II and Claim 36).

Kim et al teach a method for identifying and locating accessible sites on a target nucleic acid (Abstract and Example 2) comprising:

a) providing:

I) a target nucleic acid having at least one accessible site and at least one inaccessible site (Example 2 and Column 11, lines 4-16 and Claims 1 and 21);

ii) a plurality of extension primers, each of the primers comprising a first region, wherein the first region of the plurality of primers differ in sequence from each other, and wherein the plurality of primers comprise first regions that are complementary to different portions of the target nucleic acid, and wherein the second region is located 5' of the first region (Examples 1 and 2 and Claim 36); and

iii) a template-dependent nucleic acid extension agent (Examples 1 and 2 and , Column 11, line 30 to Column 12, line 19) ; and

Iv) an amplification agent (Examples 1 and 2 and , Column 11, line 30 to Column 12, line 19 and Claims 11-12)

b) exposing the plurality of extension primers and the extension agent to the target nucleic acid under conditions wherein primers comprising first regions that are complementary only to an inaccessible site in the target nucleic acid are not extended by the extension reagent, and wherein primers comprising first regions that are complementary to at least one accessible site of the target nucleic acid from an extension product (Examples 1 and 2 and Figure 1);

c) treating the extension products with the amplification agent and the first and second amplification primers to generate one or more amplification products, the amplification products having a length, wherein the length of the amplification products provide a distance of an accessible site on the target nucleic acid from the first domain of the target nucleic acid (Example 1 and claims 26-29 and Figure 1); and

d) determining a location of one or more accessible sites on the target nucleic acid using the distance (Examples 1 and 2 and Claims 25 and 34).

Kim et al teach a method, wherein the using the distance comprises determining the size of one or more of the amplification products (Claim 34 and Example 2).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 7-9, 19-21, and 32-34 are rejected under 35 U.S.C. 103(a) over Kim et al. (U.S.

Patent 5,846,723) (December 8, 1998).

Kim et al. teaches the method of claims 1-6, 10-18, 22-31, and 35-43 as described above.

Kim et al. does not specify the number of different primers in the range of 10 to 1000.

However, it is *prima facie* obvious that selection of the specific number of different primers represents routine optimization with regard to the requirement of screening of the number of primers and also on the length of the accessible sites of the target nucleic acids which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific number of different primers selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Response to Arguments

5. Applicant's arguments filed on April 21, 2003 have been fully considered but they are not persuasive.

Applicant argues (Page 9, fourth paragraph) that 102 rejection against claims 1-6 and 10-15 should be withdrawn because the cited reference (Kim et al. (U.s. Patent 5,846,723) does not teach the characteristic feature of the invention i.e., "identifying accessible sites on target sequences". In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "identifying accessible sites on target sequences") are not recited at least in the rejected claims 1-6 and 10-15. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant also argues (page 9, last paragraph to page 10, last paragraph) that Kim et al does not teach the main characteristic feature of the invention which is, "exposing the plurality of extension primers and the extension agent to the target nucleic acid under conditions wherein primers comprising first regions that are complementary only to an inaccessible site in the target nucleic acid are not extended by the extension agent, and wherein primers comprising first region that are complementary to at least one accessible site of the target nucleic acid form an extension product". This argument is not persuasive. Kim et al clearly teaches "exposing the plurality of extension primers and the extension agent to the target nucleic acid under conditions wherein primers comprising first regions that are complementary only to an inaccessible site in the target nucleic acid are not extended by the extension agent, and wherein primers comprising first region

that are complementary to at least one accessible site of the target nucleic acid form an extension product" (Column 13, line 49 to column 14, line 23).

Applicant also argues (Page 10, last three lines to page 11, line 14) that kim et al teaches away from the claimed invention (especially claims 28-31 and 35-43) because Kim et al uses only a pre-existing knowledge of the accessible regions of a target, whereas the claimed invention is not based on the pre-existing knowledge of the accessible regions of a target. This argument is not persuasive for three reasons. First of all, it is noted that the features upon which applicant relies (i.e., " claimed invention is not based on the pre-existing knowledge of the accessible regions of a target") are not recited at least in the rejected claims 1-6 and 10-15. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Secondly, all independent claims have the common element in section (a) "a target nucleic acid having at least one accessible site and at least one inaccessible site". It is clear from the claim language that there is some pre-existing knowledge of the target nucleic acid with regard to accessible and inaccessible regions. This trumps the attorney argument that the " claimed invention is not based on the pre-existing knowledge of the accessible regions of a target". Third reasons is, Kim et al clearly teaches, "Other accessible areas of hTR can be identified by similar assays" (Column 15, lines 31-32). Although Kim et al uses some extra method step(s) to achieve the same goal as the claimed invention, Kim clearly anticipates the claims because the open

"comprising" language of the claims permits any additional step(s) or material(s) to be added to the claimed invention.

Applicant then argues (Page 11, second paragraph) that 103 (a) rejection should be withdrawn because there is no motivation to combine the references, no reasonable expectation of success, and no teaching or suggestion in prior art of all the claim limitations. This argument is not persuasive. As clearly mentioned in the first office action that 103(a) rejection is not an obviousness rejection based on a secondary reference. It is an obviousness rejection based on "routine optimization". Therefore, no motivation is necessary to support the rejection. Secondly, With regard to the "lack of reasonable expectation of success, " argument, The MPEP 2143.02 states "Obviousness does not require absolute predictability, however, at least some degree of predictability is required. Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. In re Rinehart , 531 F.2d 1048, 189 USPQ 143 (CCPA 1976) (Claims directed to a method for the commercial scale production of polyesters in the presence of a solvent at superatmospheric pressure were rejected as obvious over a reference which taught the claimed method at atmospheric pressure in view of a reference which taught the claimed process except for the presence of a solvent. The court reversed, finding there was no reasonable expectation that a process combining the prior art steps could be successfully scaled up in view of unchallenged evidence showing that the prior art processes individually could not be commercially scaled up successfully.). See also Amgen, Inc. v. Chugai Pharmaceutical Co ., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied , 502 U.S. 856 (1991) (In the context of a

biotechnology case, testimony supported the conclusion that the references did not show that there was a reasonable expectation of success. 18 USPQ2d at 1022, 1023.); In re O'Farrell , 853 F.2d 894, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) (The court held the claimed method would have been obvious over the prior art relied upon because one reference contained a detailed enabling methodology, a suggestion to modify the prior art to produce the claimed invention, and evidence suggesting the modification would be successful.)."

There is no evidence of record submitted by applicant demonstrating the absence of a reasonable expectation of success. There is evidence in the Kim reference of the enabling methodology, the suggestion to modify the prior art, and evidence that a number of different target nucleic acid accessible sites were actually experimentally studied and found to be functional (Column 15, line 13 to 67). This evidence of functionality trumps the attorney arguments, which argues that Kim reference is an invitation to research, since Kim steps beyond research and shows the functional product.

In response to "no teaching or suggestion in prior art of all the claim limitations", it has been clearly explained as above that kim et al teaches and suggests all the claim limitations (Column 13, line 49 to column 14, line 23 and Column 15, lines 31-32).

In view of the response to arguments, all previous rejections are hereby properly maintained.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. Any inquiry of a general nature or relating to the status of this application should be directed tithe Group analyst Chantae Dessau whose telephone number is (703) 605-1237. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located In Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published In the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti

Patent Examiner

Art Unit 1634

June 18, 2003

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